

Non-Technical Abstract

This is a pilot study to evaluate the safety and feasibility of gene therapy to correct the genetic defect in the blood forming cells of patients with Fanconi Anemia. Fanconi Anemia is an inherited disorder where the body slowly stops producing blood cells which leads to life threatening anemia, bleeding and infections. The genes responsible for two forms of Fanconi Anemia have recently been identified and isolated. The normal Fanconi Anemia gene will be transferred into the blood forming cells of patients with Fanconi Anemia. This study will incorporate recent advances, which have significantly improved the ability to transfer genes into the blood producing cells of the body. Two growth factors, which normally stimulate blood production, G-CSF and SCF, will be given to patients to release high levels of blood forming cells from the bone marrow into the blood stream. These blood producing cells will be collected from patients blood with a technique called apheresis. During apheresis the patient's blood forming cells can be removed by a machine, which separates cells based upon cell size and weight. The cells which form the blood will be further purified by collecting only cells which produce the protein termed CD34 which is produced on the surface of the blood forming cells. The normal Fanconi Anemia gene will be transferred into the blood forming cells with a procedure termed retroviral mediated gene transfer. This procedure uses a part of a modified mouse virus to transfer the normal human Fanconi Anemia gene into the blood forming cells. The virus has been treated so that it cannot reproduce and make more virus. The retroviral mediated gene transfer of the blood forming cells is performed in the presence of growth factors, which normally stimulate blood forming cells to be produced, G-CSF, SCF and MGDF, and a modified form of fibronectin, a protein which helps bring the retrovirus and blood forming cells together. This study will evaluate 1) the safety of performing these procedures in patients with Fanconi Anemia, 2) whether sufficient blood forming cells necessary for transfer of the normal Fanconi Anemia gene can be collected from patients with Fanconi Anemia, 3) whether the normal gene can actually be transferred into the blood forming cells of patients with Fanconi Anemia, and 4) whether some of the abnormal properties of blood cells from patient's with Fanconi Anemia, which can be detected in the laboratory, are corrected by transfer of the normal Fanconi Anemia gene.